60 | Cranial Nerves III, IV, and VI: The Oculomotor, Trochlear, and Abducens Nerves

PART 1: CONJUGATE GAZE

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Definition

Conjugate gaze is the movement of both eyes in the same vertical or horizontal direction. Integrated supranuclear impulses produce conjugate gaze. These impulses deal with the overall function of the ocular system, not with the movement of individual extraocular muscles.

Conjugate gaze is abnormal when either or both eyes fail to move in unison in a horizontal or vertical direction. Diplopia is usually absent.

Technique

The oculomotor examination begins after examining visual acuity and visual fields. This chapter deals with the examination of five aspects of ocular function: fixation, saccadic movements, pursuit movements, compensatory movements and opticokinetic nystagmus. The monograph by Leigh and Zee (1983) and the book by Miller (1985) are excellent sources of further information.

Fixation

Have the patient look at a convenient object at 1m, and then at an object 6 m away. Carefully observe all eye movements during fixation. The ophthalmoscopic examination provides another opportunity to observe these movements. Instruct the patient to fixate on an object with the eye not being examined. Abnormal movements will be seen as motion of the optic nerve head in the eye being examined.

The eyes are never absolutely still in a normal individual. Three types of movements are seen (Miller, 1985): (1) microsaccades, occurring at a frequency of 2 per second with an amplitude of 6 minutes of arc; (2) continuous microdrift at rates of less than 20 minutes of arc/second; and (3) microtremor, which consists of high-frequency oscillations of

5 to 30 seconds of arc. The function of these movements is not clear.

Saccades

These are voluntary target-seeking or rapid eye movements. Instruct the patient to fixate alternately on two targets, such as the examiner's finger and nose. Test the movements in horizontal, vertical, and oblique directions. The patient should rapidly change fixation from one target to the other. Space the targets widely. Observe for the following:

- *Velocity:* Saccadic slowing is seen best when the patient changes fixation rapidly between two widely spaced objects.
- Time to initiate the saccade.
- Saccadic dysmetria: Note the degree of undershoot and overshoot. Both occur to a small degree in normal individuals with widely spaced targets, but rapidly diminish with repetitive refixations.

Abnormalities are usually appreciated without much difficulty at the bedside.

Pursuit Movements

These are smooth tracking movements by the eye that keep an object of interest centered on the retina. Direct the patient to hold the head still. Hold a small target about 1 m from the eyes, and move it back and forth at a slow uniform velocity. A pencil tip or swinging stethoscope will do nicely. The patient follows the object as it moves. Normal eyes will keep up with the moving object without difficulty. If the eyes do not keep up with the movement, corrective saccades will occur.

Compensatory Movements of the Vestibular System

Several bedside tests can be used to evaluate the intactness of the vestibular system (Leigh and Zee, 1983). Observe the eyes while testing for fixation (see above). Nystagmus indicates vestibular imbalance. Vestibular nystagmus is increased when fixation is removed. Consequently, note whether nystagmus is present when the eyes are closed: Palpate the movements through the lids, or watch for the lids to ripple as the eyes move.

Observe the effect of fixation during ophthalmoscopy. Watch the optic disk as the patient fixates on a distant object with the other eye. If the optic nerve head drifts, cover the other eye and note whether the drift increases when fixation is removed. Since the optic disk lies behind the center of rotation, the actual direction of drift will be opposite that perceived.

The vestibular system and related structures provide valuable information in the unconscious patient. The doll's head maneuver or caloric testing is used to test intactness of the following structures: labyrinths, eighth nerve, pontine lateral gaze centers, sixth and third nuclei, medial longitudinal fasciculus (MLF), peripheral third and sixth nerves. The reasons for testing are twofold: to test intactness of brainstem mechanisms for gaze, and to separate brainstem conjugate gaze dysfunction from cortical conjugate gaze dysfunction.

Begin with the doll's head maneuver. Hold the patient's eyes open and forcefully rotate the head from one side to the other, pausing briefly at each endpoint. A normal response is contraversive conjugate movements of the eyes; that is, the eyes rotate to the left when the head is rotated to the right. Flex and extend the neck, continuing to observe the eyes. Normally the eyes will rotate upward with flexion and downward with extension of the neck. If the results are abnormal, the caloric test must be done because it is the stronger stimulus.

The caloric test is performed using ice cold or warm (44°C) water. Using cold water is usually more convenient. First inspect the tympanic membrane to make sure it is normal. Elevate the patient's head to 30 degrees so that only the horizontal semicircular canals are stimulated. Fill an emesis basin with ice and add enough water to cover the ice. Let the water become ice cold and then draw some up in a syringe. In the conscious patient, as little as 0.5 ml is enough, while 50 ml should be used with the unconscious patient in order to be sure that a maximal stimulus is delivered. Attach a catheter to the syringe and gently inject the water into the external canal over a period of 0.5 to 1 minute. Observe the eyes for 3 minutes.

In the normal conscious patient, the elicited nystagmus has a slow and fast component. The slow component is toward the side of the injection of the cold water. This is due to brainstem mechanisms. This initial slow drift is followed by a compensatory or corrective fast component—probably of higher origin—that immediately jerks the eyes back in the other direction. Warm water produces the opposite effect: The slow component is away from the side of stimulation and the corrective fast component toward the side of the stimulation. In the conscious patient, the effects of the two components are balanced and usually the eyes remain in the midline. The mnemonic for direction of the fast phase of nystagmus in the conscious patient is COWS (Cold Opposite, Warm Same).

In the unconscious patient with a normal brainstem and vestibular system there is no fast or corrective component with cold stimulation. Since the slow component is the only one present, there is deviation to the side of the cold stimulus.

The test described above is an easily performed bedside method of testing the vestibular system. Other variants provide more subtle information; most of them require special equipment.

Convergence Movements

Convergence (vergence) or depth-tracking movements are tested by having the patient fixate on an object such as a letter 5 mm high printed on a tongue blade held at 1 m and slowly moving the object toward the patient's nose. The patient's own finger is a stronger stimulus and can be used in lethargic or inattentive patients. The point of maximum convergence is the point at which one or both eyes lose fixation and deviate outward. The location of this point is usually 8 to 10 cm, but it increases with age.

Opticokinetic Nystagmus

Opticokinetic nystagmus (OKN) is another test for measurement of ocular movements. OKN, or "railway" nystagmus, is elicited by moving test objects slowly across the field of the patient's vision. A natural example occurs when a train passenger watches telephone poles pass by the window. It is also termed the fixation reflex. Repetitive patterns on a tape or drum are satisfactory. The eyes slowly follow the object in the direction of its movement, then rapidly move in the opposite direction to pick up the next object. The pursuit system is primarily being tested. Note the regularity, smoothness, and duration of the opticokinetic response.

Basic Science

The ocular motor system has five neurologic control systems, each concerned with separate movements. These control systems exist for the purpose of keeping images stationary on the retina. In order to accomplish this, the eyes must first fixate on an object of interest, then move conjugately as the object moves or as the head moves. The five primary conjugate movements and their control systems include fixation movements, saccades, pursuit movements, vergence or depth-tracking movements, and compensatory movements (Leigh and Zee, 1983; Miller, 1985). Table 60.1 summarizes these movements.

There are three types of micromovements in normal individuals: microsaccades, continuous microdrift, and microtremor. The function of these movements is not clear. They may exist to correct minor fixation errors or to keep images from fading on the retina (Miller, 1985).

Saccades are the fastest eye movements. The word comes from the French *saquer*, which means to flick the reins of a horse or refers to the flicking of a sail in a gust of wind. Their purpose is to redirect the line of sight. The highest example of saccade is that which occurs in response to voluntary command, when the head is still. The function is to turn the eyes so the fovea will be centered on an object of interest. Saccades can be coupled with voluntary head movements. The most rudimentary saccades are those that occur as the quick phase of vestibular nystagmus during passive

Table 60.1
Neurologic Control Systems for Conjugate Gaze

Movement	Control system
1. Fixation movements (position maintenance): Minute eye movements ("micro-movements") keep the foveae fixed on the target. They are composed of small slow movements ("microdrifts") and small rapid movements ("microsaccades"). The mechanism of these movements is not worked out. It is assumed the supranuclear origin is the occipital cortex.	Occipital cortex
2. Target-tracing or pursuit movements (following movements): Once a target has been centered on the fovea, the purpose of these involuntary movements is to keep the fovea centered on the target. More specifically, the velocity of the eyes is matched to the velocity of the object of interest.	Occipital cortex: areas 17, 18, 19
3. Target-seeking or saccadic movements: These voluntary movements ("movements of command") are the fastest of all eye movements. Their function is to change the fovea of the macula from one target to another. Eye movements made in examining a scene and looking from one object of interest to several others are composed of a series of saccadic movements.	Frontal cortex: areas 8, 6, 9
4. Depth tracing or vergence movements: These movements maintain fusion of the two retinal images in spite of changes in distance between the eyes and the object. The eyes must converge as the object gets closer and diverge as it recedes.	Vergence system: areas not known for certain
5. Compensatory movements: Keeping the fovea centered on the target in spite of movements of the head.	Vestibular system: Labyrinths in the ear and vestibular nuclei in medulla. Proprioceptive receptors in the neck play a smaller role in these movements

rotation in darkness. The rapid eye movements that occur during REM sleep are also forms of saccades. All of these movements have common brainstem premotor circuits. (Some authors restrict the term saccade solely to movements under voluntary control.) The speed of the saccade is directly proportional to the distance of the movement; the larger the movement, the higher the peak velocity. A saccade accelerates rapidly, reaching peak velocity about halfway through the movement, then gently decelerates to stop abruptly. There is usually a small overshoot.

Saccades initiated for the purpose of training the fovea on a target clearly begin as a decision in higher cortical centers. A number of calculations must be made: the location of the target of interest with respect to the fovea; the location of the target with respect to the head or body; the size and velocity of saccade needed. The mechanisms whereby the nervous system converts visual sensory information into saccades are not clear. Attentional mechanisms in the parietal cortex and visual information from the occipital cortex are obviously involved. Studies indicate the nervous system continuously samples visual space with respect to saccade decision making. Visual information can be utilized for up to 70 msec before the saccade begins, this being the time it takes for the information to reach the cortex, be processed, and instructions relayed to brainstem centers. Once initiated, saccades cannot be changed in normal individuals.

Saccades under visual guidance are initiated by neurons in both the frontal eye fields and superior colliculus. Both areas have visually receptive neurons. The frontal neurons produce voluntary saccades and are concerned with maintaining visual attention. Superior colliculus neurons have to do with visual search and capture. Pathways from both regions converge upon a common saccadic pulse generator in the brainstem.

The saccadic pulse generator is located within the pontine paramedian reticular formation (PPRF), which is ventral and lateral to the medial longitudinal fasciculus (MLF). The PPRF extends from just behind the trochlear nucleus to the abducens nucleus. Three types of neurons located in the PPRF are related to saccades (Leigh and Zee, 1983):

burst neurons, pause neurons, and tonic neurons. These neurons receive commands from the cerebral hemispheres and convert them into conjugate eye movements.

Pursuit movements are necessary for objects to remain stationary with respect to the retina. The motion of objects on the retina, primarily the fovea, is probably the most important stimulus for initiation of pursuit. The best evidence is that neurons in the parietal cortex in humans are responsible for pursuit. The projection pathways to the brainstem have not been worked out. Neurons in the brainstem reticular formation, some of which are ventral to the abducens nucleus, cause the tracking movements.

Vergence movements maintain binocular fusion. The two principal stimuli are retinal blur and disparity in the location of images on the two retinas. The two eyes diverge when an object is moving away and converge when it is approaching. Experimental evidence indicates there are neurons in the visual cortex that discharge maximally when targets are located correctly in the visual fields of each eye. Experimental evidence indicates neurons in the oculomotor nucleus and in the mesencephalic reticular formation are involved in vergence movements.

The vestibular system, consisting of the labyrinth and vestibular nuclei, produces compensatory movements that keep the fovea fixed on the target in spite of movement of the head. The labyrinth, embedded in the petrous bone, contains two functional components:

1. Three semicircular canals that lie at right angles to each other. The sensory receptors in the ampulla of each canal respond to linear acceleration. The anatomic arrangement in three perpendicular planes thus permits sensing angular acceleration along three axes. Each semicircular canal influences a pair of eye muscles; for example, stimulating the left horizontal canal produces a contraction of right lateral rectus muscle and left medial rectus muscle, giving conjugate right lateral gaze. There is concomitant relaxation of the antagonist muscles, in this example the right medial and left lateral recti.

2. The utricle contains otoliths, so called because the hairs of the sensory cells stick into a gelatinous substance containing calcium carbonate crystals. The receptors respond to linear acceleration (e.g., the acceleratory forces of gravity).

Central processes from the vestibular ganglion cells project topographically onto the four main vestibular nuclei in the upper lateral medulla just below the floor of the fourth ventricle. These nuclei send efferent axons in the MLF to the brainstem nuclei of cranial nerves III, IV, and VI; these fibers are most abundant to those cranial nerve nuclei that produce horizontal and rotatory movements of the eyes. Vestibular neurons that are concerned with horizontal eye movements project primarily to the contralateral horizontal abducens nucleus. The abducens nucleus contains abducens motor neurons and abducens interneurons. The interneurons project via the contralateral MLF to the medial rectus subdivision in the oculomotor nucleus. Conjugate gaze is produced by the joint action of the abducens on one side and oculomotor nucleus contralaterally, connected via the MLF. Vestibular neurons that have to do with vertical gaze also project via the MLF to the oculomotor and trochlear nuclei.

In summary, saccades are produced by the frontal eye fields and superior colliculi, probably by parallel pathways. Contralateral saccades are produced by ipsilateral frontal eye fields or the superior colliculus. Vertical saccades occur through bilateral activity. The cortical initiation of smooth pursuit probably occurs somewhere around the parieto-occipito-temporal junction. Incompletely known pathways project to ipsilateral pontine nuclei, which then project to the ipsilateral cerebellum. The flocculus of the cerebellum appears to play a considerable role in pursuit. The vestibular system originates in the end organ, projects to the vestibular nuclei in the brainstem, and then to the nuclei of III, IV, and VI.

The brainstem converts what begins as retinal visual signals, proprioceptive impulses, and vestibular information into commands for horizontal and vertical eye movements. The brainstem takes these contributions and translates them into signals to oculomotor neurons. The input data are coded for velocity. Output by the oculomotor neurons is coded for both velocity and position. A brainstem integrator makes the conversion from one type of signal to the other, and generates appropriate horizontal and vertical conjugate movements (Leigh and Zee, 1983). This neural integrator does not have a necessary discrete location. Evidence suggests that a number of structures play a large role in its function: the cerebellum, especially the flocculus; the pontine reticular formation; and the perihypoglossal nuclei. The final location for the circuits for horizontal gaze, both saccadic and pursuit, lies in the PPRF. These neurons project to the ipsilateral abducens nucleus, and via the abducens interneurons and MLF to the contralateral medial rectus nucleus, in order to produce conjugate horizontal gaze (Figure 60.1). Cells in the rostral interstitial medial longitudinal fasciculus project to the oculomotor nuclei to produce vertical conjugate movements.

Clinical Significance

Saccadic slowing is caused by a variety of disorders (Leigh and Zee, 1983): peripheral oculomotor nerve or muscle weakness; internuclear ophthalmoplegia; PPRF lesions; a heterogeneous variety of degenerative neurologic diseases,
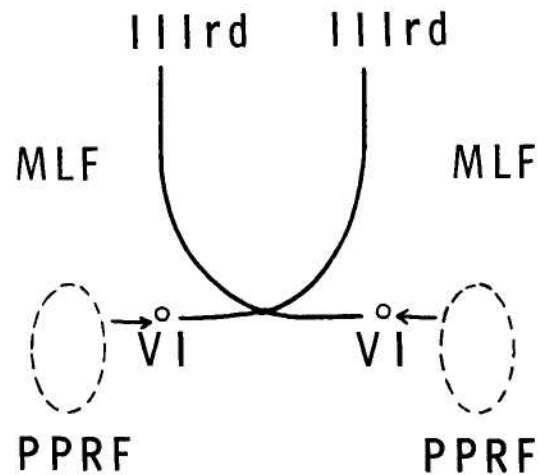

Figure 60.1
Relationships among the pontine paramedian reticular formation (PPRF), sixth nerve nuclei, medial reticular longitudinal fasciculus (MLF) and third nerve nuclei.

such as progressive supranuclear palsy. Saccadic dysmetria is seen primarily in cerebellar and brainstem lesions, and in visual defects. Problems with initiation of saccades occur in a variety of metabolic and degenerative disorders (e.g., Parkinson's disease).

Pursuit abnormalities are often due to drugs such as tranquilizers and anticonvulsants, as well as lesions of the cerebellum and its connections. Diffuse disease of one cerebral hemisphere or of one parietal lobe can produce a drift of eyes toward the intact hemisphere or parietal lobe.

Disorders of the vestibular system produce nystagmus. The characterization and analysis of nystagmus can give valuable clues to anatomical localization. There is a detailed and excellent discussion in Leigh and Zee (1983) and in Baloh (1984).

Lesions of the frontal gaze centers produce a gaze preference to one side of the body or the other. Paralysis of the left frontal gaze center produces inability of the eyes to look to the right. If the right gaze center is intact, its action will predominate, producing conjugate deviation of the eyes to the left side of the body. This condition can be distinguished from lesions of the brainstem (which also produce conjugate gaze paralysis) by stimulating the vestibular system with the doll's head maneuver or caloric test. If the brainstem is intact, the eyes will move conjugately in all directions when one of these tests is performed. A lesion of the brainstem produces a conjugate paralysis that is not overcome by the vestibular stimulus.

Focal epileptic seizures involving, for example, the left frontal gaze center, can initially produce a forced conjugate deviation to the right side of the body. With cessation of the seizure there is often a postictal paralysis of the involved gaze center. At this time the action of the opposite gaze center, if normal, will predominate. In the example given, the initial conjugate deviation to the right side of the body would be followed by conjugate deviation to the left side of the body.

Lesions of the occipital center for conjugate gaze are often associated with homonymous hemianopias. These lesions are characterized by inability of the patient to track an object and by defects in opticokinetic nystagmus.

Lesions of the MLF (which connects the sixth nucleus on one side with the third nucleus on the opposite side of the brainstem) produce paralysis of adduction. That is, the

Table 60.2
Conjugate Gaze Disorders

	Location of lesion	Clinical manifestations	Causes	Diagnosis
Lateral gaze	Hemisphere			
	Anterior (frontomes-encephalic)	Tonic deviation ipsilateral to lesion Saccadic palsy contralateral to lesion Doll's head and calorics intact	Vascular (most common) Neoplasm Demyelinating	CAT scan
	Posterior (occipitomes-encephalic)	Pursuit palsy ipsilateral to lesion Saccadic system intact Doll's head and calorics intact	Vascular Neoplasm Demyelinating	
	Brainstem: level of VIth nucleus, involving PPRF	Gaze palsy ipsilateral to lesion (both saccades and pursuit involved) Doll's head and calorics absent ipsilaterally	Vascular Neoplasm	
Vertical gaze	Brainstem structures in dorsal area of rostral midbrain on both sides	Tonic upward deviation (occulogyric crisis) Tonic downward deviation Paralysis of upward gaze (dorsal midbrain syndrome or Parinaud's): (a) paralysis of upward gaze; (b) large pupils which show light-near dissociation; (c) no vertical saccades or pursuit; (d) convergence-retraction nystagmus with attempted upward saccades; and (e) lid retraction	Parkinsonism Phenothiazines Thalamic hemorrhage or infarction Metabolic encephalopathy Pineal gland tumors Vascular Lues Rarer causes	History CAT scan Lumbar puncture
Internuclear ophthalmoplegia	MLF	Medial rectus palsy (no adduction) ipsilateral to lesion Nystagmus of the abducting eye	Multiple sclerosis Vascular infarction Tumor (Be sure to exclude myasthenia)	CAT scan Tensilon test
	MLF and PPRF: "one and a half" syndrome	Conjugate gaze palsy ipsilaterally and medial rectus palsy contralaterally	As above	As above

MLF = medial longitudinal fasciculus; PPRF = pontine paramedian reticuler formation.
Source: From Hurst JW. Medicine for the practicing Physician. Boston: Butterworths, 1983. Used with permission.

eye will not turn medially since the third nerve and therefore the medial rectus muscle has been disconnected from the lateral gaze center and sixth nucleus of the opposite side. There is usually nystagmus in the abducting eye as lateral conjugate gaze is attempted. This disconnection produces what is termed internuclear (between sixth and third nuclei) ophthalmoplegia. Multiple sclerosis and vascular lesions of the pons are two common causes.

Table 60.2 summarizes information about the more common disorders of conjugate gaze.

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_____PART 2: BRAINSTEM NUCLEI AND PERIPHERAL NERVES_____

ROBERT H. SPECTOR

Definition

In the normal cranial nerve III, the nerve function and position of eye are as follows: elevation when eye is adducted (superior rectus muscle); elevation when eye is adducted (inferior oblique muscle); depression when eye is abducted (inferior rectus muscle); adduction (medial rectus muscle); lid elevation (levator muscle); pupil constriction (pupil sphincter muscle).

Abnormal conditions involving total paralysis present with eye down and out (if fourth and sixth nerves are intact); pupil dilated and unresponsive to any stimuli; ptosis (drooping eyelid). In partial paralysis, there is a weakness or failure of any of the functions listed under normal.

Cranial nerve IV functions to depress the eye when the eye is adducted by stimulation of the superior oblique muscle. Failure of the eye to depress is an indication of paralysis. In an attempt to restore binocular vision, the patient often depresses the chin and tilts the head to the opposite shoulder.

Cranial nerve VI abducts the eye through stimulation of the lateral rectus muscle. Failure of abduction indicates paralysis.

Technique

Dysfunction of cranial nerves III, IV, and VI is recognized by identifying the paralysis of individual eye muscles innervated by these nerves. Three methods are commonly used to identify paralysis of the individual eye muscles.

Method 1: Observe the rotation of the eye in the fields of action of the appropriate muscle. Each eye is tested separately (Figure 60.2). Occlude one eye and ask the patient to fixate on a penlight or other small object. Starting with the eye in the straight-ahead position, move the fixation target slowly and horizontally in the field of action of the lateral and medial rectus muscles. Observe the range and motion of the globe. The limbus should reach the outer and inner canthus. With the eye adducted, move the target up into the field of action of the inferior oblique muscle and down into the field of action of the superior oblique muscle. With the eye abducted, move the test object up to test the superior rectus muscle and down to test inferior rectus muscle. These are the six diagnostic positions of gaze. Note that the vertically acting oblique muscles function when

the eye is adducted and the vertically acting rectus muscles when the eye is abducted.

Method 2: Comparison of rotation of yoke muscles. Yoke muscles are the pair of muscles responsible for moving the eyes in a conjugate direction. For example, the left medial rectus and right lateral rectus are yoke muscles. Innervational impulses to them are equally distributed. Ask the patient to follow an object or light as it is moved in the six diagnostic fields of gaze. Failure of one eye to follow its fellow eye indicates paralysis of the appropriate muscle of that eye. Observing the light as it is reflected on the pupil is more accurate than watching the whole globe. The normal light reflection is displaced slightly nasal to the center of the pupil. An additional maneuver is to cover one eye and watch the corrective movement of the uncovered eye. For example, if paralysis of the right lateral rectus is suspected, cover the left eye and ask the patient to follow the light into the field of action of the right lateral rectus (right lateral gaze). When the left eye is uncovered and the right eye is covered, the left eye moves briskly outward to fixate the light. The amplitude of corrective movement will be greatest in the field of action of the paretic muscle. This procedure is useful with either eye covered but is usually enhanced by using the paralytic eye for the initial fixation. In the example above, the impulses going to the right lateral rectus are equal to those going to the left medial rectus. In an attempt to move the paralyzed right lateral rectus, the impulses are increased to both eyes. The medial rectus therefore causes the left eye to move farther to the right than the partially paralyzed right eye has moved. This is known as secondary deviation.

Method 3: The red lens diplopia test. This test makes use of diplopia as a test for eye muscle weakness. The red lens over one eye enables the clinician to identify the eye to which the red image belongs. By convention the red lens is placed in front of the right eye (red is right). Hence, the red image always belongs to the right eye. A penlight and red lens are needed. Place the red lens in front of the right eye. Hold the light 60 to 90 cm in front of the patient's eyes. Ask the patient to fixate on the light; move the light into each of the six diagnostic positions of gaze. At fixation and at each gaze position ask the patient if he sees one or two images. If the patient has diplopia, he will see two lights, one red and one white. Ask the patient to tell you how far apart the images are and to describe their horizontal (right or left) and vertical (up or down) relationships to each other
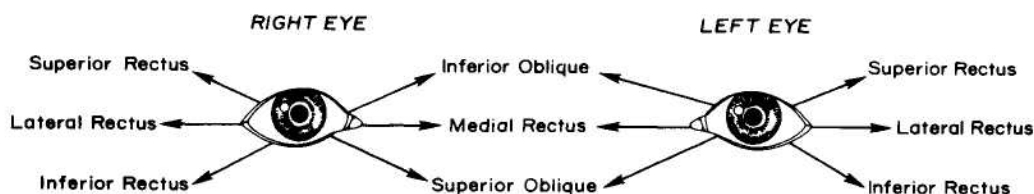

Figure 60.2
Actions of the eye muscles and diagnostic positions of gaze.

in each position of gaze. Record your findings on a chart using a solid circle to represent the red light.

This test can be interpreted as follows (red lens over right eye):

1. When the patient describes the red image to the right of the white image, there is paralysis of the right or left lateral rectus muscle.
2. When the patient describes the red image to the left of the white image, there is paralysis of the right or left medial rectus muscle.
3. The image that is displaced farthest in the direction of gaze belongs to the eye with the paralyzed muscle.

The test is most valuable in interpreting horizontal diplopia.

This test can be understood by considering the relationship of the fovea to the visual field. Any image focused on the fovea occupies the center of the visual field. Thus the eyes swing conjugately to the right in order to keep an object of interest moving to the right focused on the fovea. If a muscle of one eye is weak, that eye cannot keep up with the normal eye. The normal eye keeps the object focused on its fovea and therefore in the center of its visual field. But the weak eye loses the foveal fixation, and the visual image of the object strikes the retina peripheral to the fovea. This produces two visual images, or diplopia. The distance between these two images increases as the eyes move farther into the field of action of the weak muscle since the image in the normal eye continues to be focused on the fovea. The visual image in the weak eye gets farther from the fovea.

Consider how the images are perceived by the cortex:

1. The image focused on the fovea is localized to the center of the visual field, as noted above.
2. An image focused on the retina to the left of the fovea will be localized by the cortex to the right visual field (due to the reversal of image by the lens).
3. An image focused on the retina to the right of the fovea will be localized by the cortex to the left visual field. Figures 60.3 and 60.4 demonstrate the use of the test to detect a lateral medial rectus paralysis and a right superior oblique paralysis.

A summary of the findings in some examples in which the red lens is over the right eye are:

1. On right lateral gaze the red image is to the right of the white image: paralysis of the right lateral rectus. This follows the guidelines that when the red image is to the right of the white image there is paralysis of the right or left lateral rectus muscle. The right eye and, therefore, the right lateral rectus is involved since the red image is farthest in the direction of gaze.
2. On left lateral gaze the red image is to the left of the white image: paralysis of the right medial rectus. Since the red image is to the left, one of the medial recti is involved. The right medial rectus is the culprit since the red image is farthest in the direction of gaze.

Additional tests include:

1. Head tilt test for fourth nerve paralysis. Tilt the head first to one shoulder and then to the other. Observe the amount of vertical separation of the eyes or of the diplopic images. The greatest separation occurs
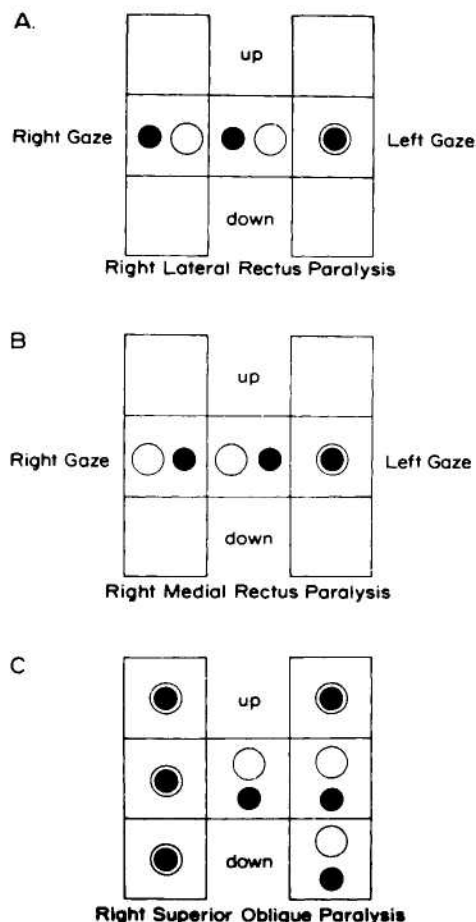

Figure 60.3
Examples of red glass diplopia tests. The red lens is over the right eye and the red image is indicated by the solid circle.

with the head tilted to the same shoulder as the side of paralysis.
2. Position of the head. Head position often gives a clue to a paretic ocular muscle. Head tilted to the shoulder and chin down are seen with superior oblique muscle paralysis opposite the direction of the tilt. The head is turned away from the side of a lateral rectus paralysis.
3. Examining the function of the superior oblique muscle in the presence of total third nerve paralysis. When the third cranial nerve is paralyzed, the eye cannot be adducted; hence, the depression of the globe in adduction (field of action of the superior oblique) cannot be performed. One should look for the secondary action of the superior oblique, which is rotation of the globe. Ask the patient to look in the direction that would normally adduct the paretic eye. Observe a conjunctival vessel nasally while asking the patient to look up and down. On down gaze the eye can be seen to rotate inward if the superior oblique is functioning.

Basic Science

The *oculomotor nerve* arises from a paired group of motor cells extending approximately 5 mm in length just beneath the central gray substance of the mesencephalon, at the level
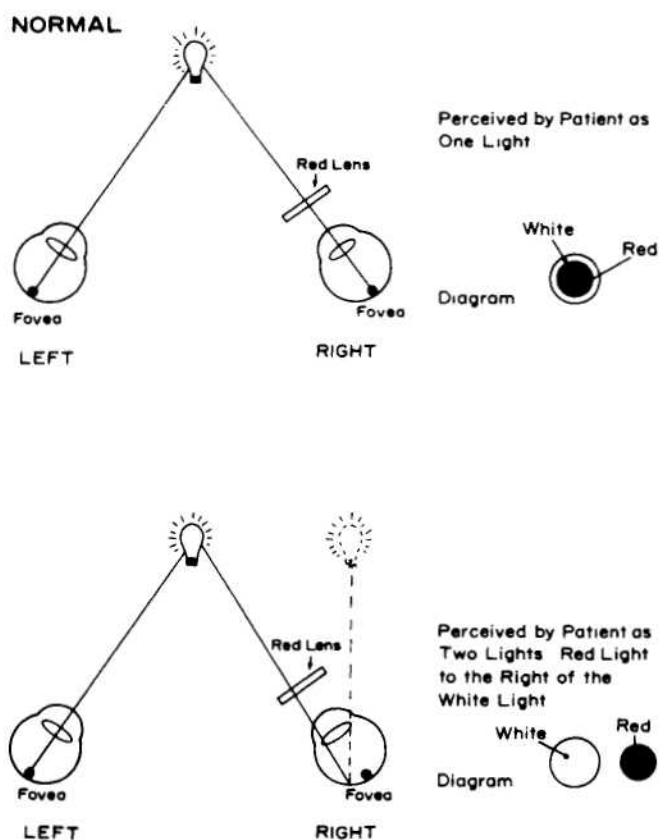
NORMAL

Perceived by Patient as
One Light

Red Lens

White
Red

Diagram

Fovea   Fovea

LEFT   RIGHT

Perceived by Patient as
Two Lights   Red Light
to the Right of the
White Light

Red Lens

White   Red

Diagram

Fovea   Fovea

LEFT   RIGHT

Figure 60.4
Explanation of red lens diplopia test.

of the superior colliculi. Axons from the nuclei pass ventrally through the red nucleus to exit the midbrain in the interpeduncular fossa. Passing forward through the subarachnoid space, the third nerve lies adjacent to the posterior communicating artery and punctures the posterior wall of the cavernous sinus just lateral to the posterior clinoid. Within the cavernous sinus, it assumes a superolateral position and anteriorly bifurcates into a superior and inferior division. The superior division supplies the superior rectus and the levator palpebrae superioris muscles. Branches from the inferior oculomotor division provide innervation to the medial rectus, inferior rectus, and inferior oblique muscles along with parasympathetic axons to the pupilloconstrictor muscle of the iris and the ciliary body.

The oculomotor nuclear complex has been studied extensively by Warwick. The following points deserve special emphasis: Both lid levators are served by a single dorsal-caudal midline nucleus; the motor cell pool of the superior rectus muscle sends fibers across to the opposite oculomotor nerve to supply the contralateral superior rectus muscle; a nucleus for convergence has not been consistently demonstrated in primates, including humans; at the caudal aspect of the oculomotor complex is the trochlear nucleus, whose axons turn dorsally to cross in the anterior medullary velum and innervate the contralateral superior oblique. Therefore, the nuclear pools of the superior rectus and superior oblique muscles are contralateral to the eye they move.

The *trochlear nerve* exits the midbrain dorsally and crosses the contralateral fourth nerve in the anterior medullary velum just caudal to the inferior colliculi. The fourth nerve

is the only cranial nerve to exit the brain dorsally. It continues laterally around the midbrain tectum, crosses the superior cerebellar artery, and reaches the free edge of tentorium, where it enters the dura and runs forward into the cavernous sinus. The fourth nerve enters the orbit through the superior orbital fissure to supply the superior oblique muscle.

The *abducens nucleus* is situated in the caudal portion of the pontine tegmentum beneath the floor of the fourth ventricle. Efferent axons pass ventrally through the corticospinal tract to emerge from the brainstem at the lower border of the pons in the pontomedullary sulcus approximately 1 cm from the midline. The nerve ascends the ventral surface of the pons for a short distance, is crossed by the anterior and inferior cerebellar artery, and pierces the dura of clivus approximately 2 cm below the posterior clinoid. Here, it pierces or passes above the inferior petrosal sinus, runs beneath the petroclinoid ligament, and enters the cavernous sinus. Passing just lateral to the carotid artery and medial to the third, fourth, and ophthalmic divisions of the trigeminal nerve, the abducens nerve eventually traverses the cavernous sinus and superior orbital fissure to innervate the lateral rectus muscle.

Clinical Significance

Oculomotor Nerve

Based on Warwick's scheme of the third nerve nuclear complex, the following rules apply to the clinical diagnosis of nuclear third nerve lesions:

1. Conditions that *cannot* represent nuclear lesions:
   a. Unilateral external ophthalmoplegia (with or without pupil involvement) associated with normal contralateral superior rectus function
   b. Unilateral internal ophthalmoplegia
   c. Unilateral ptosis
2. Conditions that *may be* nuclear:
   a. Bilateral total third nerve palsy
   b. Bilateral ptosis
   c. Bilateral internal ophthalmoplegia
   d. Bilateral medial rectus palsy
   e. Isolated single muscle involvement, except the levator and superior rectus muscles
3. *Obligatory* nuclear lesions:
   a. Unilateral third nerve palsy with contralateral superior rectus palsy and bilateral partial ptosis
   b. Bilateral third nerve palsy (with or without internal ophthalmoplegia associated with spared levator function)

Axons from each subnucleus of the oculomotor complex pass anteriorly through the medial red nucleus and cerebral peduncles. Nerve fascicles from each nucleus are anatomically separate from each other within the midbrain, so fascicular lesions frequently produce partial oculomotor dysfunction. If the ipsilateral red nucleus is simultaneously involved, there is a tremor of the contralateral extremities (Benedikt's syndrome). More ventral lesions with involvement of the corticospinal tract cause a spastic hemiparesis contralateral to the third palsy (Weber's syndrome). The most common causes of midbrain fascicular third nerve palsies include stroke, trauma, and, on rare occasions, brain tumors.

Third nerve damage in the interpeduncular or subarachnoid space generally causes *total* third nerve paralysis. There is complete ptosis and a complete inability to rotate the eye upward, downward, or inward. The ipsilateral pupil is large and unreactive to a light or near stimulus and there is paralysis of accommodation. Traumatic third nerve damage and aneurysms of the posterior communicating artery are the most common causes of acute, spontaneous, and complete unilateral oculomotor paralysis. While most patients with cerebral aneurysms present with intense headache, stupor, or coma, many will be awake, lucid, and pain free. Pain by itself, regardless of its severity, does not distinguish clearly between a third nerve palsy caused by a cerebral aneurysm and the nonsurgical causes of acute oculomotor palsy. The pupillary response to light remains the most reliable way of differentiating between conditions.

Therefore, the term "pupillary sparing" needs precise definition. True pupillary sparing should be limited to the clinical situation where there is complete ptosis and paralysis of ocular elevation, depression and adduction, but normal pupillary size and movement. Normal or near-normal pupillary reactivity with partial ptosis and/or partial ophthalmoparesis does not constitute true pupillary sparing because this condition simply represents partial third nerve palsy with partial pupillomotor dysfunction. The patient presenting with a true pupil-sparing third nerve palsy rarely harbors an intracranial tumor or aneurysm. Such patients, in the author's opinion, can be followed clinically if their state of consciousness is normal. Provided the pupil retains normal size and reactivity after 1 week of observation, these patients need not undergo CT or cerebral angiography.

Hypertension, diabetes, and other types of small vessel disease cause true pupil-sparing oculomotor palsies. In this syndrome pain may be prominent, but usually resolves within 3 or 4 days; the ophthalmoplegia *always* resolves within 3 to 4 months. Clinicopathologic studies of such patients have revealed swelling of the subarachnoid or intercavernous portion of the third nerve, hyalinized vessels supplying the swollen segment of nerve and ischemic infarction of the nerve core itself.

Not all patients with true pupil-sparing third nerve palsies have vascular, self-limiting conditions because lesions of the cavernous sinus and superior orbital fissure also can cause normal pupillary movement. But, as stated above, these patients will usually have *partial* weakness of other oculomotor nerve structures. Since the oculomotor nerve bifurcates into superior and inferior divisions within the cavernous sinus or superior orbital fissure, relative pupillary sparing may in part reflect sparing of the inferior division that also innervates the medial and inferior rectus and inferior oblique muscles. It may be explained by the fact that pupillomotor fibers, in the process of joining the twig to the inferior oblique muscle, may either assume an independent course or descend from the vulnerable superficial position in the subarachnoid portion of the nerve to a relatively more protected position within the substance of the nerve or on its lateral or inferior surface. Cavernous sinus involvement of the third nerve can be differentiated from more proximal oculomotor lesions by accompanying signs that point to involvement of contiguous anatomic structures, namely the sixth, fifth, fourth, and sympathetic nerves.

Trochlear Nerve

Closed head trauma is by far the most common cause of unilateral or bilateral fourth nerve palsies. Isolated fourth nerve weakness may also occur in patients with hypertension and/or diabetes or, on rare occasions, it may be a sign of a space-occupying lesion within the brainstem. A Tensilon test should always be performed in a patient with an isolated superior oblique palsy if there is no recent history of head trauma and no documentation of hypertension or diabetes.

Abducens Nerve

Because the causes of sixth nerve palsy are legion and the evaluation of such patients is extensive and expensive, the examiner should first rule out causes of "pseudo-sixth nerve palsy." Conditions that also produce abduction failure include Duane's syndrome, spasm of the near reflex, myasthenia gravis, and thyroid ophthalmopathy. Duane's syndrome is a congenital and usually unilateral abduction deficit that most often occurs in females. During the attempt to abduct the affected eye, there is concomitant widening of the ipsilateral palpebral fissure. Ocular adduction is accompanied by narrowing of the palpebral fissure and retraction of the globe. Duane's syndrome is reportedly related to congenital atresia or absence of ipsilateral sixth nerve; the denervated lateral rectus muscle is reinnervated by a twig of the oculomotor nerve.

Spasm of the near reflex is a functional disorder of eye movement. During lateral gaze, the patient superimposes ocular convergence. For instance, when the patient gazes to the left, the right and left eyes initially move to full extent until the patient converges. At that point, the right eye remains adducted, but the left eye floats medially, simulating abduction failure. The true diagnosis is established by observing pupil size, as the act of convergence also produces miosis. In true abduction palsy, the pupil size remains constant.

Myasthenia can present as an isolated eye muscle palsy and thus mimics sixth nerve palsy. Any patient with unexplained double vision, especially of a fluctuating nature, should be considered a myasthenic suspect and should undergo Tensilon testing. The physician should not rely solely upon subjective improvement of diplopia after Tensilon administration. Objective measurement of diplopia with prisms and the cross-cover test before and after drug administration are better suited for this purpose.

Restrictive eye movement caused by pathologic changes in extraocular muscles secondary to entrapment or dysthyroidism can also cause abduction limitation. The extraocular muscles in dysthyroid ophthalmopathy are usually enlarged, firm, and rubbery owing to interstitial edema, endomysial fibrosis, and a heavy infiltrate of collagen, mucopolysaccharides, lymphocytes, and plasma cells. The added bulk physically enlarges the eye muscles and tethers the globe. This results in variable degrees of primary position strabismus and/or incomplete ocular ductions and versions. Severe involvement of the medial rectus muscle, for example, fixes the globe to a medial position. With less extensive myopathy, the eyes may be straight in primary position and move normally across the horizontal plane, but a small esotropia is present in lateral gaze. Both of these clinical situations—mimicking gross and minimal abduction palsy, respectively—warrant the force ductions tests. Failure of the examiner to move the globe in the direction of ocular paresis indicates inelasticity of the antagonist eye muscle, not weakness of the agonist eye muscle. Such restriction related to fibrosis, entrapment, or direct infiltration of the muscle itself is most commonly caused by thyroid ophthalmopathy.

Once the diagnosis of true sixth nerve palsy is established, various etiologies should be considered depending upon the site of the culpable lesion. Patients with intraparenchymal sixth nerve disease will usually show signs of involvement of contiguous anatomic structures. In close proximity to the sixth nerve nucleus and fascicles are the facial and trigeminal nerves, corticospinal tract, median longitudinal fasciculus, and the paramedian pontine reticular formation. A combination of clinical findings pointing to involvement of these structures signals the presence of an intrapontine lesion.

The peripheral course of the abducens nerve is a lengthy one, which predisposes it to involvement by lesions at all levels, from the brainstem and base of the skull, through the petrous tip and cavernous sinus, to the superior orbital fissure and orbit. As the nerve ascends the clivus it may be involved by intraforaminal extension of nasopharyngeal carcinoma, clivus chordoma, or other neoplasms in the prepontine basal cistern. In addition, basal forms of meningitis (sarcoidosis, tuberculosis, cryptococcus, and carcinomatosis) frequently produce unilateral or bilateral sixth nerve palsies as an early sign.

Before entering the cavernous sinus, the abducens nerve crosses the medial aspect of the petrous bone. During the preantibiotic era, severe and unrelenting middle ear disease would frequently lead to petrous osteomyelitis. Children would present with a combination of severe pain in the trigeminal distribution and ipsilateral sixth nerve palsy (Gradenigo's syndrome).

Lesions of the cavernous sinus produce polyneuropathic ophthalmoparesis. There is usually a mixture of sympathetic third, fourth, sixth, and fifth cranial nerve involvement. Anterior cavernous sinus or superior orbital fissure lesions with mixed ophthalmoparesis will generally show moderate to severe proptosis. Bilateral polyneuropathic extraocular muscle palsies may be seen in the following situations: the Guillain-Barré syndrome, infiltrative brainstem tumors, extension of nasopharyngeal carcinoma along the base of the skull, carcinomatous meningitis of the basal meninges, sarcoidosis, clivus chordoma, pituitary apoplexy with extra-extracellular extension of the pituitary tumor into one or both cavernous sinuses, sphenoid carcinoma, cavernous sinus thrombosis, and many forms of carotid-cavernous fistulas. These diverse clinical situations can be differentiated by their temporal course, physical findings, and radiological evaluations.

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